REMARKS

Claims 1-24 are pending in the present application. Claims 15-24, have been withdrawn as being directed to non-elected subject matter. Claims 1-4, 6-14 are currently under examination..

The rejection if claims 1-14 under 35 U.S.C. § 101 is withdrawn. The rejection of claims 1-14 under 35 U.S.C. § 112, first paragraph, is withdrawn. The objection to the disclosure, specifically the brief description of drawings because of minor informalities is withdrawn. The objection to claims 1, 7, 10, 13 because of minor informalities over notation is withdrawn. The rejection of claim 5 under 35 U.S.C. § 112, second paragraph, as being indefinite is withdrawn. The rejection of claim 10 under 35 U.S.C. § 102 (b) as being anticipated by Lemanski *et al.*, (1996 *Biochem. Biophys. Res. Comm.* 229:974-981) is withdrawn.

Maintenance of Objections and Rejections

Claims 1-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 7, 10, 13 are drawn to a purified nucleic acid comprising a nucleotide sequence that encodes a MfR molecule. The Examiner rejects the claims based on the word "encodes" and "functional activity." The Examiner asserts that it is unclear what the activity of RNA is. The Examiner has included Claims 4, 6, 8-9, 11-12, 14 in the rejection "because they are dependent on the above claims." Applicants respectfully traverse.

Applicants describe, for example, on page 24, lines 5-35, that culturing of adult mutant sheep hearts in the presence of the RNA molecules of the invention, rescued the mutant hearts which developed vigorous rhythmic beating. It is implicit in this that the RNA does have a functional activity, which could be for example, binding to a molecule, stabilizing a molecule etc.

Applicants therefore, disclose that the molecules are useful in treating heart disease by restoring heart muscle. The functional activities of the MIR-encoding nucleic acids, disclosed in the instant invention, include: binding to MIR proteins, induction of rhythmic contraction, myofibrillar induction, induction of differentiation of a cell into cardiac muscle phenotype.

The functional activities associated with the MIR encoding nucleic acids are summarized by applicants on page 9, lines 1-15:

> Myofibrillogenesis inducing RNA (MIR) is an RNA molecule expressed in embryonic endoderm, with the ability to induce formation of myofibrils in differentiating cardiomyocytes of normal, but not mutant individuals, in an animal model of heart development.
>
> In studies disclosed herein, the full-length nucleotide sequence of MIR is disclosed. It is further shown that MIR extracted from adult mammalian (sheep) heart has the ability to **promote ("rescue") heart cell differentiation** in mutant salamanders, enabling these cells to exhibit **normal rhythmic contractions, tropomyosin distribution, and myofibril formation.** Detection of **RNA-protein interactions** by Northwestern blotting and gel-shift assays further led to the isolation of two MIR-binding proteins having molecular weights (MW) of about 13-15 kDa and about 28-30 kDa. Comparison of MIR DNA sequences from normal and mutant embryos revealed a point mutation in the mutant DNA that resulted in the loss of functional (rescue) ability of the RNA, coupled with inability to bind the larger MW MIR-binding protein. Taken together, these results demonstrate that myofibrillogenesis and promotion of a normal cardiac muscle phenotype can be achieved through the interaction of **MIR RNA with one or more MIR-binding proteins.** (Emphasis added).

Applicants submit that the invention describes the "functional activities and the claims are therefore, not indefinite.

Applicants have amended the claims to remove reference to the term "encodes" and substituted the time "is transcribe" as per the Examiner's recommendation. These amendments are not to be construed as surrender of any subject matter and applicants hereby reserve the right to pursue the subject matter in one or more Continuation or Divisional applications.

Claim 7 was rejected for reciting the phrase "shares sequence identity." The Examiner asserts that the claim is indefinite "because it is unclear what 'shares sequence identity' means."

Applicants describe the meaning of "sequence identity." See, for example, page On page 10, lines 26-28 through to page 11, lines 1-9, Applicants teach that the 5' untranslated region shares a 100% identity with :an RNA splicing factor:

> In another aspect, the invention includes nucleic acids in the form of myofibrillogenesis-inducing ribonucleic acid (RNA) molecules (MIR) that are encoded by the DNA molecules of the invention and by definition are complementary to the DNA molecules. The RNA molecules of the invention are shown herein to have bioactive properties such as 1) inducing heart beating and myofibrillogenesis in the muscle cells of embryonic hearts and 2) binding to specific MIR-binding proteins. The latter interaction is thought to promote transcription of genes, such as tropomysosin, associated with muscle cell differentiation. Additionally, it is shown herein that a fragment of a MIR-encoding cDNA (i.e., SEQ ID NO:6) shares **100% identity with a sequence in the 5' untranslated region of the axolotl homolog of SmN, an RNA splicing factor** (Huntriss JD et al., 1993. Nucleic Acids Res. Aug 25;21(17):4047-53), **further supporting a role for MIR in regulation of muscle cell differentiation**. In preferred embodiments, the MIR molecules of the invention are between about 167 and about 620 nucleotides in length. (Emphasis added).

On page 32, lines 25-28 through to page 33, lines 1-12:

> Example 16- Sequence Homology of MIR with a 5' Untranslated Region of axoSmN cDNA
>
> In related studies, a full length cDNA encoding the axolotl homolog of the mammalian SmN, termed herein "axoSmN," was cloned. The mammalian SmN gene encodes a tissue-specific RNA slicing factor (Huntriss JD et al., 1993; Gerrelli D et al., 1994). Of note, comparison of the MIR cDNA sequence with the axoSmN sequence revealed an exact match of a portion of the MIR sequence (i.e., GCC GAT CCT TTG GAA TTT GTA CAT GTG ACC TCA AGG TTG CAC GCA TAT CCG AGC AGT TGC TGG ATT AGA GCA GGC ACT CCC TTG) (SEQ ID NO:6) with an identical sequence in the 5' untranslated region of the axoSmN gene. Referring to FIG. 7, the positions of these residues in the MIR cDNA sequence are indicated in italics. Referring to FIG. 8, a full-length cDNA sequence for axoSmN is shown. The underlined sequence in the 5'-untranslated region of axoSmN is the sequence exhibiting 100% sequence identity with a portion of the MIR cDNA. The shaded portion of the AxoSmN sequence represents a large deduced open reading frame showing homology to the mammalian SmN gene. Poly (A) tail and polyadenylation signal (in bold) are also indicated. **The finding of the common sequence in MIR and**

> **axoSmN points to a potential relationship between MIR and the axoSmN gene, possibly through common interacting proteins.** (Emphasis added).

Thus, Applicants describe the term "sequence identity." However, in order to expedite prosecution, Applicants have amended the claim to remove reference to the phrase "sequence identity." As such the amended claim 7 to identify that SEQ ID NO: 5 contains an identical sequence corresponding to the 5' untranslated region of a second nucleic acid that encodes an RNA splicing factor, as identified by SEQ ID NO's: 6 and 7. Support for this amendment is shown above.

Claim 10 was rejected for the term "as identified by SEQ ID NO: 5. In response, Applicants have amended claim 10 to remove reference to said term as SEQ ID NO: 5 is identified in claim 1. Claim 10 has also been further amended to correct certain grammatical errors. No new matter has been added by virtue of these amendments and their entry is respectfully requested.

Claims 1-3, 7, 10 and 13 are rejected under 35 U.S.C. § 112 second paragraph. The rejection is based on the term "encodes." In response, Applicants have amended the claims.

In view thereof, Applicants submit that claims 1-14 are allowable under 35 U.S.C. § 112, second paragraph. Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim Rejections Under 35 § U.S.C. 103(a)

Claims 13-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lemanski *et al.* (1996 *Biochem. Biophys. Res. Comm.* 229:974-981).

As the Examiner has acknowledged, Lemanski *et al.*, do not teach "a nucleic acid as identified by SEQ ID NO: 5."

Applicants reiterate that Applicants disclose a full length sequence of a MIR-encoding nucleic acid molecule (SEQ ID NO.: 5), including sequences that are equal to or greater than 166 nucleotides in length. Furthermore, applicants teach the importance of the secondary structure of the MIR-encoding molecule and functions associated therewith. (See above). Applicants teach the importance of a point mutation that destroys the functions of SEQ ID NO.: 5. See figure 5. Although the sequence of clone #4 is embedded in the MIR-encoding molecule, the sequence identified in Lemanski *et al.*, does not correspond to the sequence identified by the instant invention and **would not posses the secondary structure of the full length MIR-encoding molecule** as taught by Applicants.

Also, as discussed by applicants on page 33, lines 1-12, and shown in figure 8A, the SmN as represented by SEQ ID NO's.: 6 and 7 are not taught nor disclosed by Lemanski *et al.* SEQ ID NO's.: 6 and 7 do not match up to the clone #4 sequence shown in Figure 1 of Lemanski *et al.* In addition to the foregoing, the claims, as amended, precludes any teaching or suggestion by Lemanski *et al.*

However, to expedite and compact prosecution Applicants have amended the claims to recite SEQ ID NO: 5. Lemanski *et al* neither teach nor disclose this sequence, nor could one of ordinary skill in the art identify this sequence by reading the cited reference, and as such cannot be obvious.

It is respectfully submitted that for the foregoing reasons, claims 13 and 14 are patentable over the cited reference and satisfy the requirements of 35 U.S.C. §103. As such, these claims are allowable.

CONCLUSION

In view of the foregoing, reconsideration and withdrawal of all rejections and allowance of the application is respectfully solicited. Applicants respectfully request entry of the foregoing amendments and remarks and reconsideration and withdrawal of all rejections. If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants'

attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at telephone number shown below.

Although, Applicants believe that no further extensions of time (beyond the one month petition) are required with submission of this paper, Applicants request that this submission also be considered as a retroactive petition for any extension of time if necessary. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,

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Date: May 8, 2006

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